

PATENT COOPERATION TREATY

REC'D 21 FEB 2005

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From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/US2004/034501

International filing date (day/month/year)
20.10.2004

Priority date (day/month/year)
31.10.2003

International Patent Classification (IPC) or both national classification and IPC
A61K31/44, C07D213/30, C07D213/61, A61P1/04

Applicant
ASTRAZENECA AB

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/034501

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
 - This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - a sequence listing
 - table(s) related to the sequence listing
 - b. format of material:
 - in written format
 - in computer readable form
 - c. time of filing/furnishing:
 - contained in the international application as filed.
 - filed together with the international application in computer readable form.
 - furnished subsequently to this Authority for the purposes of search.
3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/034501

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application,
 claims Nos. 12, 13

because:

- the said international application, or the said claims Nos. 12, 13 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
 the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
 no international search report has been established for the whole application or for said claims Nos.
 the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

- the written form has not been furnished
 does not comply with the standard
the computer readable form has not been furnished
 does not comply with the standard

- the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
 See separate sheet for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US2004/034501

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or
Industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims 6-8, 11-13
	No:	Claims 1-5, 9, 10
Inventive step (IS)	Yes:	Claims 6-8, 11-13
	No:	Claims
Industrial applicability (IA)	Yes:	Claims 1-11
	No:	Claims

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2004/034501

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 12 and 13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Prior art

Reference is made to the following documents:

D1: WO 03/013247
D2: WO 02/28182
D3: US 2003/204090
D4: TETRAHEDRON LETTERS vol. 32, no. 6, 1991, pages 811-814
D5: WO 02/062323
D6: WO 01/16121
D7: WO 99/02497

2 Novelty (Article 33(2) PCT)

2.1 The present compounds claimed in claims 1-4 overlap with the compounds disclosed in D1 and D2 (see D1, claim 1, formula I and D2, claim 1, formula I) and do not appear to relate to any new technical teaching. Numerous examples specifically disclosed in D1 and D2 fall within the claimed scope.

4-Prop-2-ynyoxybenzonitrile disclosed in D3 (see D3, page 31, [0297]) and compound 3 of D4 (see D4, page 812) fall within the claimed scope.

Hence D1-D4 are prejudicial to the novelty of claims 1-4.

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- 2.2 The compounds claimed in claims 1-4 are novel over D5-D7 at least due to their propinyloxy linker. Although there exist an overlap between the present compounds of claims 1-6 and those disclosed in D6 (see D6, formula I with L is alkynylene and B is substituted hydrocarbyl) said propinyloxy linker represents a new technical teaching over D6.
- 2.3 The intermediates claimed in claim 11 are not specifically disclosed in the cited prior art. Present claim 11 is therefore novel.

3 Inventive step (Article 33(3) PCT)

3.1 Claims 1-10, 12 and 13

D5-D7 which disclose compounds useful for treating disorders mediated by the metabotropic glutamate receptors represent the closest prior art. The D5 and D7 compounds differ from the present compounds in view of their propinyl linker between the pyridine ring and phenyl ring (see also item 2.2). Although a formal overlap exists between the present compounds and those disclosed in D6, all exemplified compounds of D6 equally miss said linker. Hence, the scope of D6 appears so speculative that the skilled person would not have seriously contemplated the present compounds as compounds useful for treating disorders mediated by the metabotropic glutamate receptors. Inventive step is acknowledged for the present compounds which are delimited from the prior art.

3.2 Claim 11

An inventive step can be acknowledged for the intermediates claimed in claim 11 since they make a structural contribution which differentiates the subsequent products from known compounds of the relevant prior art i.e. (part of) the linker mentioned above.

4 Industrial applicability (Article 33(4) PCT)

For the assessment of the present claims 12 and 13 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The

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patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

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